Retinoic Acid-Mediated Cytotoxicity of the Human Umbilical Cord-derived mesenchymal Stem Cells

Farnoosh Saraee[1], Homa Kochesfahani[2], Masoud Maleki[3], Mohsen Sagha[4]

1. Department of Animal Sciences, School of Life Sciences, University of Kharazmi, Tehran, Iran
Research Laboratory for Embryology and Stem Cells, Department of Anatomical Sciences and Pathology, Faculty of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran
2. Department of Animal Sciences, School of Life Sciences, University of Kharazmi, Tehran, Iran
3. Department of Biology, Sciences and Research Branch, Azad Islamic University, East Azerbaijan, Tabriz, Iran
4. Research Laboratory for Embryology and Stem Cells, Department of Anatomical Sciences and Pathology, Faculty of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran

Background and Aim:
Retinoic acid (RA), a derivative of vitamin A, has a key role in vision, the immune system, reproduction, the differentiation and proliferation of cells and as a biological factor affects on normal embryonic development. Both excess and deficiency of RA may result in birth defects. A couple of studies report that excessive doses of RA, teratogenically induce malformations in different embryological organs including limb buds. Using the human umbilical cord derived stem cells (HUCSCs) as an in vitro model of human fetal cells we aimed to evaluate cytotoxicity effects of retinoic acid on human embryo.
Methods:
Human umbilical matrix derived mesenchymal stem cells (HUCSCs) were cultured in DMEM+10% FBS at a density of 1×10^3/well. Upon adhering onto the culture dish and entering of cells in the logarithmic phase of growth, the medium was changed to DMEM containing different concentrations of RA for 4-6 days during which RA refreshed every 2 days. The cells cultured without RA were considered as a control group. Five days post-treatment, cell proliferation was measured by using the MTT colorimetric assay and morphology of apoptotic cells was detected with Acridine orange/Ethidium Bromide staining.
Results:
Cell proliferation was significantly decreased in the cells exposed to high doses of RA (10^{-7}-10^{-5} M) compared to control group. Fluorescence staining also revealed that RA- treated cells had a blebbed morphology and DNA fragmentation.
Conclusions:
This study clearly shows that RA in a dose-dependent manner had a cytotoxicity effect on HUCSCs.

Keywords: Retinoic acid, Human umbilical cord derived stem cells, cytotoxicity, cell proliferation,

Corresponding Author:
Mohsen Sagha: m.sagha@arums.ac.ir